REMARKS

Claim 1 has been amended to specify that the surface polymeric material has nano-sized surface features that comprise a dimension within the range of about 25 nm to less than 100 nm. Support for the amendment to claim 1 is found throughout the specification, including for example, on page 4, lines 23-27. Claim 2 is amended to state that the surface features are formed by chemical treatment and claim 4 recites various chemicals that are used in accordance with one embodiment. In addition, claim 3 is amended to specify one group of polymeric materials that are suitable for use in the present invention. Support for the amendment to claims 2, 3 and 4 is found throughout the specification, including for example, on page 3, lines 11-24.

Claim 12 is amended to specify that the composition is a polymeric film comprised of poly(lactic-glycolic acid) and arginine-glycine-aspartic acid peptides. Support for that amendment is found on page 9, lines 25-26. Claim 13 is amended to specify extracellular matrix components suitable for use with the claimed invention. Claim 14 is amended to further specify that the implant comprises an extracellular matrix component from bladder smooth muscle cells. Claims 14-16 have been amended to specify the location of the extracellular matrix components on, or within, the implant. Support for the amendments to claims 13-16 is found through out the specification including, for example, original claims 13 and 14 and on page 8, lines 23 through page 9, line 2.

New claims 33-42 have been added. Claims 33-36 specify suitable compounds that can be used as the extracellular matrix component in accordance with the present invention. Support for those new claims is found in original claims 15-17 and page 8, line 23 through page 9, line 13. Claim 37 is directed to a nano-structured synthetic implant for repair of soft tissues, said implant consisting of a polymeric material and a population of cells. Support for new claim 37 is found throughout the specification, including for example, at page 3, lines 1-19 and page 9, lines 14-15. Claims 37-41 are directed to a nano-structured synthetic implant comprising a polymeric material having nano-sized surface features comprising peaks and valleys. Support for the new claims 37-41 is found throughout the specification, including for example at page 4, lines 23-32 and page 5, lines 20-21. New claim 42 is directed to an implant formed by a molding process, and support for that claims is found on page 10, lines 15-20.

Applicants acknowledge and confirm their election of the Group I invention (claims 1-20). Claims 21-32 directed to non-elected subject matter have been cancelled.

Specification Objections

The Examiner has objected to the Abstract for including a second paragraph. Applicants have amended the specification to remove the second paragraph. The amendment to the Abstract is believed to fully address the Examiner's objection, and applicants respectfully request the withdrawal of the objection to the Abstract.

Information Disclosure Statement Objection

The Examiner has requested the full citation of the reference listed as "DU" on page 4 of the IDS. The full citation is as follows: Paul Weiss, "Experiments on Cell and Axon Orientation in Vitro: The role of Colloidal Exudates in Tissue Organization," Journal of Experimental Zoology, vol. 100(3), (1943), pgs 353-386. Applicants submit herewith a substitute sheet listing the full citation of the "DU" reference.

Claim Rejections

Claims 1-5, 10-16 and 18-20 stand rejected under 35 USC § 102(e) as being anticipated by Webster (US Patent No. 6,270,347, the "'347 patent"). Applicants respectfully traverse this rejection.

Claim 1 of the present invention is directed to a nano-structured synthetic implant for the repair of soft tissues, wherein the implant comprises a polymeric material having nano-sized surface features. The '347 patent is directed to nano-grained ceramic compositions for orthopaedic-dental implants. The '347 patent is devoid of any teaching with regards to a composition that comprises a nano-textured polymer and thus fails to anticipate the polymeric compositions of the present invention. However, to advance the prosecution of the present application, claim 1 has been amended to incorporate the limitation of claim 6, thus obviating the rejection. Accordingly, applicants respectfully request the withdrawal of the rejection of claims 1-5, 10-16 and 18-20 as being anticipated by Webster.

Claims 1-4, 6-7, 10-16 and 18-20 stand rejected under 35 USC § 102(e) as being anticipated by Hammerick (US 2002/0173033). Applicants respectfully traverse this rejection.

Claim 1 has been amended to specify that the nano-structured synthetic implant comprises surface features having at least one dimension ranging in size from about 25 to less than 100 nanometers. Hammerick fails to teach a composition having a nano-scale dimension (i.e., less than 100 nm). Accordingly, Hammerick fails to teach the claimed

invention as amended herein. Therefore, applicants respectfully request the withdrawal of the rejection of claims 1-4, 6-7, 10-16 and 18-20 as being anticipated by Hammerick.

Claims 1 and 6-8 stand rejected under 35 USC § 103 as being obvious over the teachings of Webster (US Patent No. 6,270,347). Applicants respectfully traverse this rejection.

Webster is directed to nanostructure ceramics for oethopaedic /dental applications. The reference fails to teach or suggest an implant suitable for use with soft tissues, wherein the implant comprises a polymeric material that displays nanotextured surface features having at least one dimension in the range from about 25 nm to about 100 nm and a surface roughness of greater than 50nm.

The Examiner contends that the '347 patent teaches a composition comprising a polymer with nano-sized surface features. However, applicants believe the Examiner is overstating the teachings of the '347 patent and note that a careful reading of that document reveals that the reference discloses a "a nanocomposite of one or more nanostructured ceramic, having a grain size of 1-100nm and at least one of an adhesion-promoting peptide and a non-peptide polymer". (see column 4, lines 49-53). Accordingly, the reference fails to teach a composition comprising a polymeric material wherein the polymeric material itself displays nano-sized surface features and a surface roughness of about 50 nm or greater.

The '347 patent discloses compositions that comprise nano-structured ceramic materials. While the '347 composition may further comprise polymeric material, the reference fails to teach or suggest a composition comprising nano-structured polymeric materials. In this regard applicants note the preparation of the nano-grained ceramic materials of the '347 patent is conducted by forming precipitates of the ceramic materials using controlled reactions. There is no disclosure relating how to prepare polmeric materials that display nano-textured surfaces. Accordingly, the '347 patent fails to teach or suggest the desirability of a composition comprising nano-structured polymeric materials, and furthermore, the reference is devoid of any guidance of how prepare such polymeric materials that display nano-sized surface features and a surface roughness of about 50 nm or greater.

Applicants note that claim 2 has been amended to specify one manner in which nano-textured polymeric materials can be prepared. More particularly, claim 2 specifies that the implants are comprised of polymers that have been chemically treated to produce dimensions in the range from about 50 nm to less than about 100 nm. Applicants respectfully submit that such chemical treatment modifies the structure of the polymers by altering not only their physical shape (e.g. providing nano-scale roughness) but also by changing surface

reactivities. Surface reactivities of the implant are altered by chemical treatments resulting in changes to the percentages of elemental composition, or the percentages of certain chemical functional groups, relative to those exhibited by conventional polymeric materials. Such changes can alter the overall surface properties including for example the wettability of the implant. Accordingly, the chemical treatment process step imparts structural limitations to the implant. The '347 patent fails to teach or suggest polymeric materials modified by such chemical treatments and accordingly the invention of claim 2 is even further removed form the teachings of the '347 patent.

The Examiner contends that one of ordinary skill in the art would have been motivated to optimize the specific surface roughness of the implant. However, even if applicants accept that statement, the '347 patent only discloses modified ceramic surfaces and is devoid of any suggestion regarding the modification of any polymer component that is also present in the composition. The '347 patent simply fails to consider or suggest that a polymer surface should be modified to display nanotextured surface. Thus there is no motivation to "optimize" the surface roughness of polymers used in implant compositions. Accordingly, Webster fails to teach or suggest applicant's claimed implant that has been designed for use with soft tissues such as bladder tissue.

To further distinguish the present invention over the compositions disclosed in the '347 patent, new claim 33 has been added and specifically excludes the inclusion of ceramic materials in the presently claimed invention. All compositions disclosed in the '347 patent comprise a ceramic component (i.e., alumina, titania or hydroxyapatite). The '347 patent fails to teach or suggest an implant that lacks the ceramic supporting structure. There is simply no suggestion in the '347 patent that an implant lacking such material could be prepared and have the requisite strength required for the uses disclosed in the present application.

Accordingly, Webster fails to teach or suggest the present invention and applicants respectfully request the withdrawal of the rejection of claims 1 and 6-8 as being obvious over the teachings of Webster (US Patent No. 6,270,347).

Claims 1, 5, 8-9 and 17 stand rejected under 35 USC § 103 as being obvious over the teachings of Hammerick (US 2002/0173033). Applicants respectfully traverse this rejection.

Hammerick is directed to a multi-layered device that provides for three-dimensional spatial localization of cells. Similar to the constructs disclosed in the cited Webster reference, the Hammerick devices require the inclusion of a support layer in addition to numerous "containment layers". The support layer "is typically a piece of flat material such as glass, Pyrex, quartz, polydimethylsiloxane, biocompatible silicone based polymer,

biocompatible metal or polymer, silicon, hardened polymer, titanium, porous material, film, which may have a smooth surface or etched surface to facilitate assembly and stability of the device." (paragraph 0088 of Hammerick). New claim 33 excludes such materials, and accordingly, is patentably distinct over the compositions disclosed by Hammerick.

Applicants also note that Hammerick is directed to compositions that comprise submicron surface features, but fails to teach or suggest a composition comprising a polymeric material displaying nano-sized surface features, wherein said surface features comprise a dimension having a size within the range of about 25 nm to less than 100 nm. As disclosed on page 4, lines 8-12 and in Example 11, and more particularly on page 24, lines 24-29 of the present specification, polymeric materials displaying surface features of less than 100nm (i.e. nanometer range) showed surprising superiority to submicron (i.e., 100 nm to 1 um) textured surfaces in terms of bladder smooth muscle adhesion. Hammerick fails to teach or suggest any compositions comprising polymeric materials that display surface features having a dimension less than 100nm (i.e., 0.1 um). Applicants have found that preparing polymer surface features that go below the 100nm cutoff produces significant and surprising results. In further support of the significance of the 100nm cutoff value, applicants have provided a Declaration under 37 CFR 1.132 of Dr. Webster and accompanying additional experimental data.

Chemically-treated and cast nanostructured poly(lactic-co-glycolic acid) (PLGA) and polyurethane (PU) films (having surface feature dimensions less than 100nm) were prepared and compared to chemically-treated and cast submicron poly(lactic-co-glycolic acid) (PLGA) and polyurethane (PU) films (having surface feature dimensions of 100 nm to 1 μm) to determine the relative protein bioactivity of the two surfaces. The results shown in Exhibit A (attached to the Declaration under 37 CFR 1.132, submitted herewith) show greater competitive fibronectin and vitronectin adsorption, as well as RGD exposure in proteins, on both chemically-treated and cast nanostructured PLGA and PU compared to respective conventional (untreated) and sub-micron polymers (Figure 1 for PLGA and Figure 2 for PU in Exhibit A). Sub-micron polymers were observed to have the same degree of protein adsorption and bioactivity as conventional polymers. Importantly, fibronectin and vitronectin are essential cell adhesive proteins and RGD is a key cell adhesive domain in proteins. Accordingly, applicants have discovered that a relatively small reduction in the size of surface features on polymeric materials, moving from submicron dimensions of 100nm to 1um to nanometer dimensions of 25-100nm (produced either by chemically-treatment or cast)

can surprisingly promote bioactive protein adsorption and conformation significantly beyond that obtained using sub-micron or conventional surface polymers.

There is simply no suggestion within Hammerick that producing polymeric materials displaying nano-sized surface features having a size within the range of about 25 nm to less than 100 nm would have a significant effect on protein and cell interactions with the polymer compositions. Furthermore, Hammerick is devoid of any teaching or suggestion that their constructs could be subjected to chemical treatments to alter the physical properties of the polymeric materials.

The Examiner contends that one of ordinary skill would have been motivated to "optimize" the surface features of the Hammerick constructs. However, applicants respectfully submit that a particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). Contrary to the Examiner's assertion, the Hammerick specification at paragraph 0042 states, "'Well' means a selectively designed topological feature on the surface of the containment layer in the nanometer, micrometer or millimeter range. The well may be of any size, depending on whether one cell, several cells, cluster of cells or piece of tissue is deposited there." Accordingly, applicants respectfully submit that Hammerick fails to place any significance on the size of the surface features of their devices (other than in reference to gross capacity) and fails to indicate that such a parameter is a "results-effective variable"

Furthermore, even if the size of the surface features of a polymeric material were known to be a result-effective variable, the discovery of a new effective range is nonobvious when the results obtained using the new range are unexpectedly good. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). As disclosed in the present specification, and the Declaration by Dr. Webster (with accompanying further experimental data), polymeric surfaces displaying surface features having dimensions less than 100nm display unexpected properties relative to the properties displayed by compositions that have submicron or larger surface features. When an applicant demonstrates substantially improved results and states that the results were unexpected, this should suffice to establish unexpected results in the absence of evidence to the contrary. *In re Soni*, 54 F3d 746 (Fed. Cir. 1995). The existence of novel or superior unexpected properties, undisclosed by the prior art, weighs heavily in favor of a conclusion that the claimed composition is not obvious. *Air Products and*

Chemicals, Inc. v. Chas S. Tanner Co., 219 USPQ 223, 231 (SC 1983); *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987).

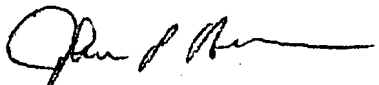
Applicants have discovered the surprising result that compositions that display surface features having a dimension of less than 100nm have dramatically improved desirable properties relative to surfaces displaying submicron surface features. There was simply no reasonable expectation that such an effect could be achieved prior to applicants' invention, and Hammerick provides no motivation for preparing such compositions.

Accordingly, Hammerick fails to teach or suggest applicant's claimed polymeric implant, having nanotextured surface features and designed for use with soft tissues such as bladder tissue. Therefore, applicants respectfully request the withdrawal of the rejection of claims 1, 5, 8-9 and 17 as being obvious over the teachings of Hammerick (US 2002/0173033).

Claims 1-12 stand provisionally rejected based on nonstatutory obviousness-type double patenting as being unpatentable over claims 1, and 7-20 of co-pending Application No. 10/362,148. In addition, claims 1-12 and 18 stand provisionally rejected as being unpatentable over claims 1-11 of co-pending Application No. 10/793,721. Applicants respectfully request that these rejections be held in abeyance until the Examiner makes a finding of patentable subject matter.

The foregoing claim amendments and remarks are believed to fully respond to the Examiner's rejections, and the claims are believed to be in condition for allowance. Applicants respectfully request allowance of the claims, and passage of the application to issuance. If any further discussion of this matter would speed prosecution of this application, the Examiner is invited to call the undersigned at (434) 220-2866.

Respectfully submitted,



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